REMARKS

Claims 49, 57 and 58 were pending in the subject application, with claims 1-48, 50-56 and 59-78 having previously been canceled, without prejudice or disclaimer. By this Amendment, claims 49 and 58 have been amended to clarify the claimed subject matter, and new claim 79 has been added. Claims 49, 57, 58 and 79 would be pending upon entry of this amendment, with claim 49 being the sole pending claim in independent form.

Applicant submits that no new matter has been introduced by this Amendment. Support for the claim amendments can be found in the application as originally filed, for example, at page 10, lines 2-8, page 12, line 30 through page 13, line 13, page 29, lines 12-23 and page 33, lines 1-15. Accordingly, Applicant respectfully requests that this Amendment be entered.

Rejections Under 35 U.S.C. § 102

In section 4 of the September 24, 2009 Office Action, claims 49, 57 and 58 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Hollis et al. (US 5,846,708).

Applicant respectfully submits that the present application is allowable over the cited art, for at least the reason that the cited art does not disclose or suggest the aspects of the present application of a method for analyzing a sample oligonucleotide seguence including … **contacting the sample oligonucleotide sequence with the anchor sequences and with a *mobilized* probe,** wherein the probe comprises an oligonucleotide sequence which hybridizes to a target oligonucleotide sequence to be detected in a suitable buffer, to form a complex … .

Such aspects are discussed in the present application, such as, for example, at page 12, lines 30-page 12, line 13 (reproduced below):

> "...*this invention features a method for concentrating and reacting analytes or reactants at any specific micro-location on the device. After the attachment of the specific binding entities, the underlying microelectrode at each microlocation continues to function in a direct current (DC) mode. This unique feature allows relatively dilute charged analytes or reactant molecules free in solution to be rapidly transported, concentrated, and reacted in a serial or parallel manner at any specific micro-locations which are maintained at the opposite charge to the analyte or reactant molecules. Specific micro-locations can be protected or shielded by maintaining them at the same charge as the analytes or reactants molecules. This ability to concentrate dilute analyte or reactant molecules at selected microlocations greatly accelerates the reaction rates at these micro-locations*".

The present application (page 29, lines 12-23) further states:

> "*The improvements in these reaction parameters come from the ability of the device to electronically control and affect: (1) the rapid transport of reactants or analytes to a specific micro-location containing attached specific binding entities; (2) improvement in reaction rates due to the concentrated reactants or analytes reacting with the specific binding entities at that specific micro-location; and (3) the rapid and selective removal of un-reacted and non-specifically bound components from that micro-location. These advantages are utilized in a novel process called 'electronic stringency control*".

The aforementioned aspects enable significant improvements in reaction rates, specificities and sensitivities, in comparison to conventional methods such as the method of Hollis. The mobilized probe in such aspects hybridizes with a sequence of the target oligonucleotide that is other than the sequence hybridized with a complementary anchored sequence (see, e.g., page 33, lines 1-15, of the present application).

Further, as discussed in the present application (page 10, lines 2-8), the mobilized probe can be concentrated together with the sample oligonucleotide sequences to thereby significantly improve the reaction rates, specificities and sensitivities.

Hollis, as understood by applicant, proposed a microelectronic sensor array for RNA and DNA sequencing, as shown in Figure 1 (reproduced below) of Hollis, wherein the sequencer 10 includes an X-Y array of test sites 12 electronically addressable by conductive leads X1, X2, .. XN on the X-axis and conductive leads Y1, Y2, .. YN on the Y-axis, and in addition, X-logic circuitry 36 is provided for sequentially addressing each X-line and is coupled to detection and recognition circuitry 40, and similarly Y-axis circuit 56 is coupled to the Y-lines. The test sites 12 are formed in a semiconductor wafer using semiconductor photolithographic processing techniques.

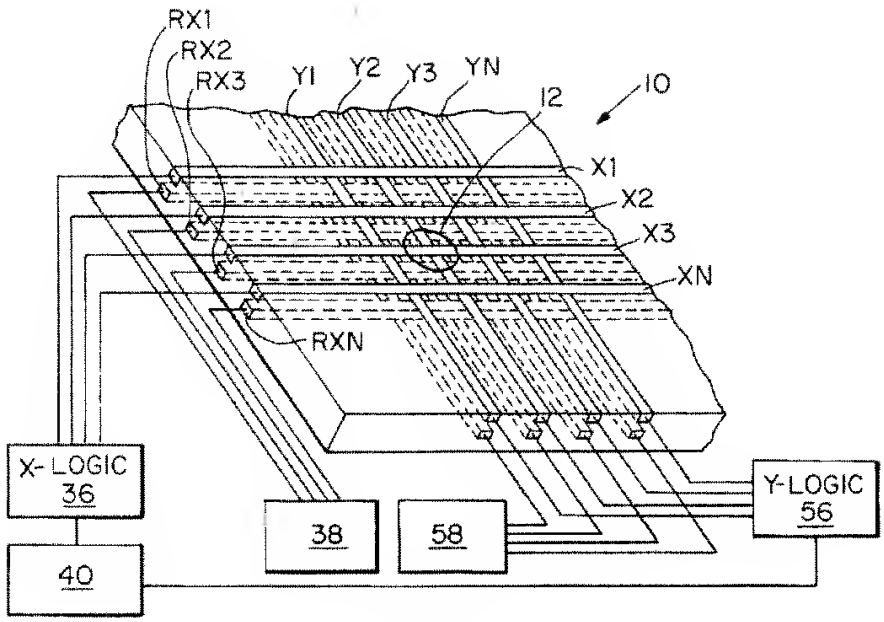

Fig. 1

Each test site contains a plurality of probes 22, shown in Fig. 4 (reproduced below) of Hollis, which are capable of binding to known molecular structures or "targets", e.g. polynucleotides, DNA, RNA, cells, antibodies or anti-antibodies. When a sample substance containing the targets in an electrolyte solution 18 is poured onto the array 10, the targets bind with associated probes 22 within a plurality of wells 42 formed in each test site 12.

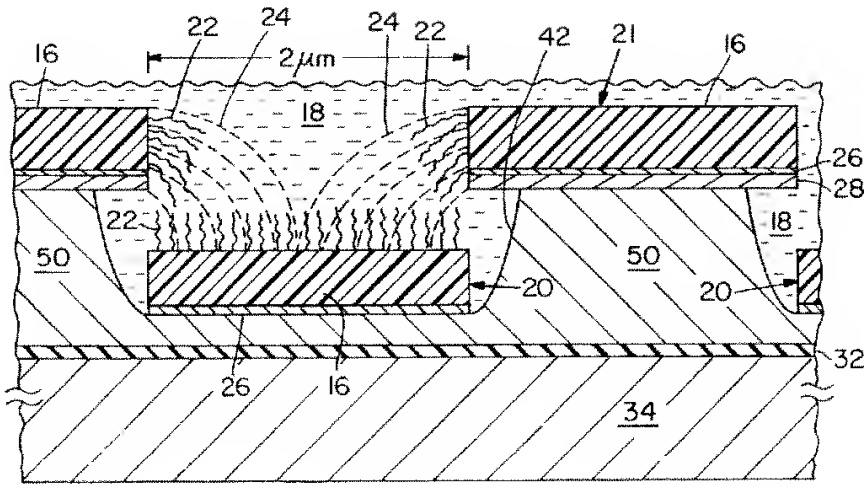

Fig. 4

The targets contained in the electrolyte solution 18 of Hollis are apparently equated in the Office Action to a sample oligonucleotide sequence.

Hollis states on col. 10, line 65 through col. 11, line 1 that "The probes [22] are attached to the test sites by fixation to a solid support substrate on the surface of the wells 42, or alternatively, attached directly to the electrodes 16 or 20, as in Fig. 4".

Accordingly the approach proposed in Hollis, as understood by applicant, uses a probe capable of binding to a specific molecular structure ("target") in a sample oligonucleotide sequence in which the probe is attached to a test site by fixation to a solid support substrate (i.e. immobilized), and when a sample substance containing the target in an electrolyte solution is poured onto the array, said target binds with said associated probe.

Hollis does NOT teach or suggest the aforementioned aspects of **contacting the sample oligonucleotide sequence with the anchor sequences and with a *mobilized* probe**, wherein the probe comprises an oligonucleotide sequence which hybridizes to a target oligonucleotide sequence to be detected in a suitable buffer, to form a complex.

Applicant submits that the cited art, even when considered along with common sense and common knowledge to one skilled in the art, does ***NOT*** render unpatentable the aforementioned aspects of the present application.

Accordingly, applicant submits that amended claim 49 and the claims depending therefrom are allowable over the cited art.

Withdrawal of the rejection under 35 U.S.C. § 102 is requested.

Double Patenting Rejection

In section 6 of the September 24, 2009 Office Action, claims 49, 57 and 58 were rejected on the ground of nonstaturtory obviousness-type double patenting as purportedly unpatentable over claims 1-12 of U.S. Patent No. 6,051,380.

Claims 1-12 of U.S. Patent No. 6,051,380 are reproduced below:

> 1. A method for transport and hybridization of DNA in an active electronic system comprising the steps of:
> providing a low conductivity, zwitterionic buffer on said device,
> electrophoretically transporting said nucleic acid towards a microlocation,
> applying current and voltage to the microlocation to effect transportation, whereby the local pH above the microlocation is below the pH of the buffer at its isoelectric point, whereby hybridization between the nucleic acid and a probe located at the microlocation is enhanced.

2. The method for enhanced transport and hybridization of nucleic acids of claim 1, wherein the low conductivity, zwitterionic buffer is histidine.

3. The method for enhanced transport and hybridization of nucleic acids of claim 1, wherein the low conductivity, zwitterionic buffer is L-histidine.

4. The method for enhanced transport and hybridization of nucleic acids of claim 1, wherein the low conductivity, zwitterionic buffer is D-histidine.

5. A method for the effective transport and hybridization of DNA on an active, electronic matrix device, the device having a plurality of microlocations, at least certain of the microlocations including probes, comprising the steps of:

providing a first low-conductivity, zwitterionic buffer to the device,

providing said nucleic acids to the device in said low conductivity, zwitterionic buffer,

applying current and potential to at least certain microlocations so as to effect transport of said nucleic acids to selected microlocations,

changing the buffer to a second buffer with a high salt concentration, and

effecting hybridization of said nucleic acid with said probe at selected microlocations.

6. The method for effecting transport and hybridization of nucleic acids of claim 5, wherein the low conductivity, zwitterionic buffer is cysteine.

7. The method for effecting transport and hybridization of nucleic acids of claim 5, wherein the low conductivity, zwitterionic buffer is alanine.

8. The method for effecting transport and hybridization of nucleic acids of claim 5, wherein the salt concentration is from approximately 50 mM to 100 mM.

9. A method for detection of point mutations in double stranded amplicons comprising the steps of:

providing amplicon products to an active, programmable electronic matrix device,

dilute said products in a low conductance histidine buffer,

denature said products,

hybridize said denatured products in the histidine

buffer on the device,

perform stringency so as to discriminate matches versus mismatches, and

detect and analyze said products.

10. The method of claim 9 for detecting point mutations in amplicons wherein the stringency includes electronic stringency.

11. The method of claim 9 for detecting point mutations in amplicons wherein the detection is fluorescent detection.

12. The method of claim 9 for detecting point mutations in amplicons wherein a fluorescent reporter probe sequence is hybridized with said product.

Applicant respectfully points out that claims 1-12 of U.S. Patent No. 6,051,380 do not disclose or suggest various aspects of the present application, such as, for example:

(a) forming a plurality of microscopic locations on a substrate, wherein each microscopic location is individually electronically addressable;

(b) electronically immobilizing one or more anchor sequences to individually selected microscopic locations;

(c) contacting a sample oligonucleotide sequence with the anchor sequences and with a mobilized probe, forming a complex; and

(d) subjecting said complex to an electric field which moves unbound oligonucleotide sequences away from said anchor sequences in the direction of said field.

Accordingly, withdrawal of the obviousness-type double patenting rejection is requested.

In view of the amendments to the claims and remarks hereinabove, applicant submits that the application is allowable. Applicant earnestly solicits the allowance of the application.

No fee, other than the $555.00 three-month extension of time fee, is deemed necessary in connection with the filing of this Amendment. However, the Patent Office is hereby authorized to charge any additional required fees in connection with this Amendment, and to credit any overpayment during prosecution of this application, to our Deposit Account No. 03-3125.

If a telephone interview could advance the prosecution of this application, the Examiner is respectfully requested to call the undersigned attorney.

Respectfully submitted,

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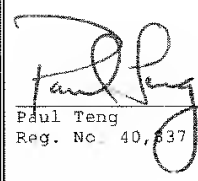

March 24, 2010

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Date